measurable response when brought in contact with a corresponding substrate and a promoter comprising no more than two cAMP response element (CREs). Claim 40 has been amended to recite a cDNA or mRNA expressing human TSH-R stably transfected with a reporter construct comprising cDNA of both a reactant capable of causing a measurable response when brought into contact with a corresponding substrate, and a promoter comprising no more than two cAMP response elements (CREs). The levels of the reactant also vary with the induced endogenous cAMP levels.

Support for the recitation of a "promoter" may be found on page 3, lines 12-13 of the present specification. Support for the recitation that the promoter comprises no more than two CREs may be found generally throughout the specification. Specifically, the Examiner's attention is respectfully directed to page 11, lines 25-30 and the examples which utilize no more than two CREs.

Applicants believe that the proposed combination of LUDGATE et al. in view of HIMMLER et al. fail to disclose or suggest the claimed invention. LUDGATE et al. is directed to a bioassay for detecting autoantibody agonists and antagonists directed against a TSH-R. The TSH-R is coupled to the cAMP transduction pathway and therefore activity/binding at the TSH-R can be monitored through measuring cAMP levels. LUDGATE et al. describe a bioassay in which cloned cells, transfected to express human TSH-R, are exposed to patient's samples and the presence of

autoantibodies is assessed by detecting the levels of cAMP in the system. The levels of cAMP are measured using a radio immune assay which can take several days to perform. However, LUDGATE et al. fail to disclose or suggest the claimed clone, cDNA or mRNA set forth in the claimed invention. In an effort to remedy the efficiencies of LUDGATE et al., the Official Action cites HIMMLER et al.

HIMMLER et al. describe assays for testing human dopamine D1 and D5 receptors expressed in stable cAMP-responsive luciferase reporter cell lines. HIMMLER et al. note that the activity of the receptor coupling to the cAMP signal transduction pathway is measured via transcriptional activation of a reporter gene. In the study, a Chinese hamster ovary cell line was stably transformed with a reporter plasmid containing the firefly luciferase gene under the transcriptional control of multiple cAMP responsive elements (CREs).

On page 84, HIMMLER et al. state that they tested the reporter plasmid with various combinations of CRE sequences in order to obtain the highest transcriptional induction rates in transient transfection asays. HIMMLER et al. clearly state that a plasmid containing six heterologous CRE sequences (derived from bovine leukemia virus LTR, vaso active intestinal peptide, somato statin and cytomegalo virus) upstream of a minimum β-globin promoter (Figure 1A) gave higher induction rates than constructs with three identical or different CRE sequences.

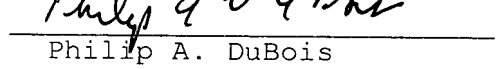
Applicant respectfully submits that this passage teaches away from the claimed invention. As noted above, the claimed invention is directed to no more than two CREs. Thus, while HIMMLER et al. may disclose that three identical or different CRE sequences may be used, HIMMLER et al. clearly teach the desirability of using six or more sequences. Even if one of ordinary skill in the art were to combine the cited publications, one of ordinary skill in the art would still not obtain the claimed invention. Thus, upon reviewing the cited publications, one of ordinary skill in the art would lack the motivation to combine and modify the teachings to obtain the claimed invention.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 36, 38-40, 42, 44 and 45, as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

YOUNG & THOMPSON

By 

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January 27, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amend claim 36 as follows:

--36. (twice amended) A clone expressing human TSH-R (thyotropin receptor) stably transfected with a reporter construct comprising cDNA of both

(i) a reactant capable of causing a measurable response when brought into contact with a corresponding substrate, [such as a protein]

and

(ii) a promoter comprising no more than two [containing] cAMP response elements (CREs), [comprising a promoter sequence or synthetic oligonucleotide which contains the CRE consensus sequence, TGACGTCA,]

whereby levels of the reactant vary with induced endogenous cAMP levels[; and

wherein the promoter sequence or synthetic oligonucleotide is that for the glycoprotein hormone alpha subunit that contains a tandem repeat of the CRE consensus sequence, TGACGTCA].--

Amend claim 40 as follows:

--40. (twice amended) cDNA or mRNA expressing human TSH-R (thyotropin receptor) stably transfected with a reporter construct comprising cDNA of both

(i) a reactant capable of causing a measurable response when brought into contact with a corresponding substrate, [such as a protein]

and

(ii) a promoter [containing] comprising no more than two cAMP response elements (CREs),

[comprising a promoter sequence or synthetic oligonucleotide which contains the CRE consensus sequence, TGACGTCA,]

whereby levels of the reactant vary with induced endogenous cAMP levels[; and

wherein the promoter sequence or synthetic oligonucleotide is that for the glycoprotein hormone alpha subunit that contains a tandem repeat of the CRE consensus sequence, TGACGTCA].--